# SCH- GLUCOTRAXPEPT CAP

## NEXT GENERATION ENCAPSULATED ACTIVES

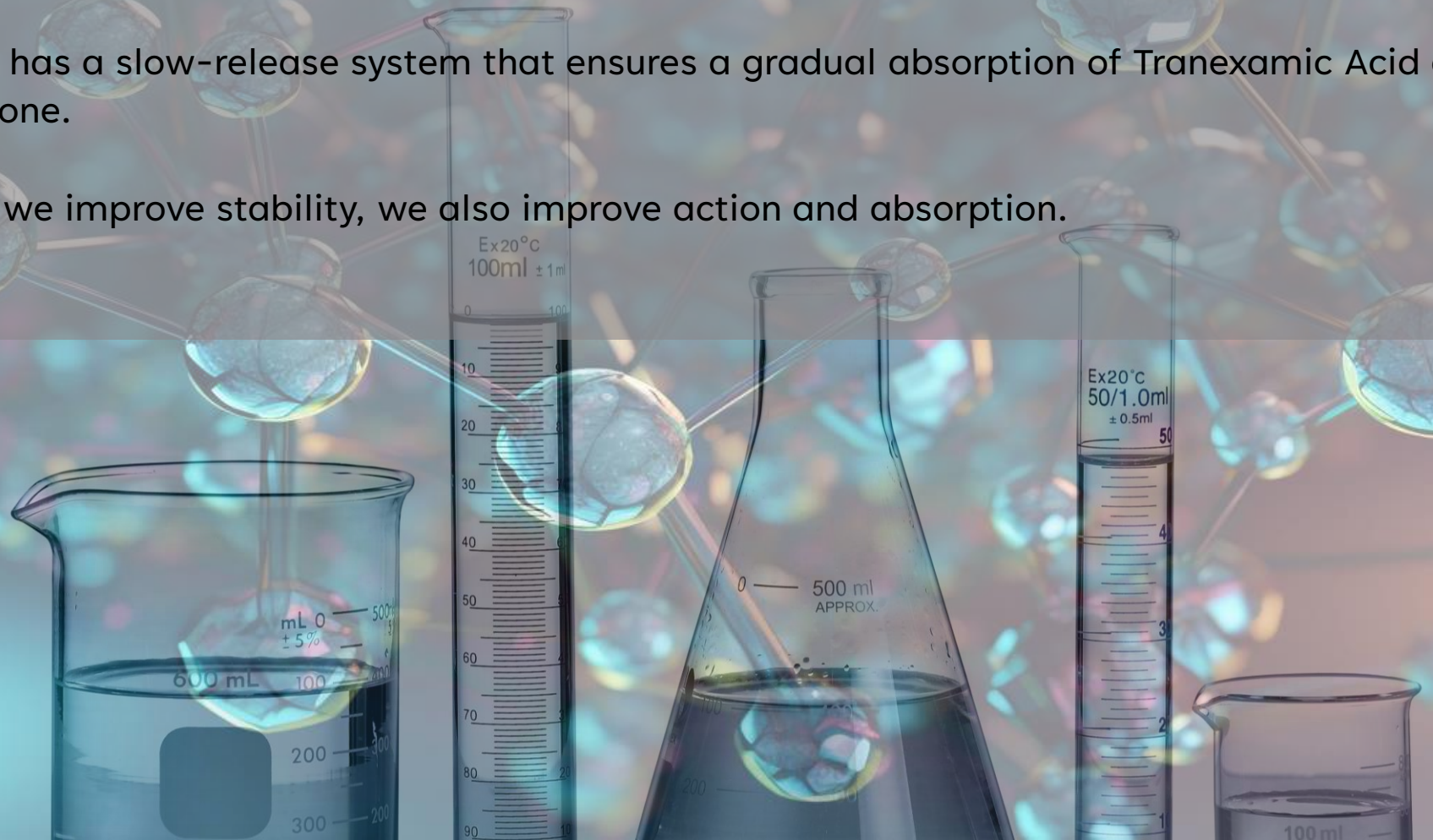
Developments of new cutting-edge peptide-based drugs and molecules with pharmacological, diagnostic and cosmetic interest.

Special Chemicals

# SCH- GLUCOTRAXPEPT CAP

A new encapsulation technology allows Tranexamic Acid and Gluconolactone to penetrate deeper into the skin.
The capsule has a slow-release system that ensures a gradual absorption of Tranexamic Acid and Gluconolactone.

Not only do we improve stability, we also improve action and absorption.



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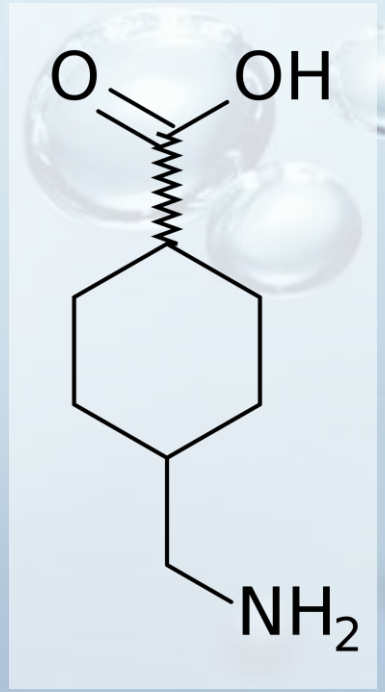
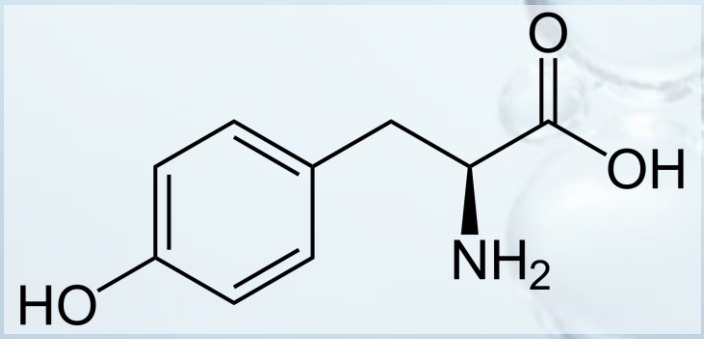
STRUCTURE OF TRANEXAMIC ACID




STRUCTURE OF TYROSINE




Tranexamic acid also is known as a pharmaceutical agent. Already in 2011, it has been entered on the "Model List of Essential Medicines" (EML) of the World Health Organisation (WHO) - in particular for the treatment of trauma after traffic accidents or in the case of haemorrhagic risks and even fatal haemorrhage. Tranexamic acid (= International Nonproprietary Name, INN), from the chemical viewpoint, is an amino acid, and more precisely, we are speaking of trans-4-(aminomethyl) cyclohexanecarboxylic acid.

A chance discovery for dermatology: In dermatology the effects of tranexamic acid have been known for a long time, namely in the context of pigment disorders. The first report on the treatment of melasmas with tranexamic acid dates back to 1979 and comes from an accidental observation after the oral administration of tranexamic acid. In the particular case, the intensity of a melasma was significantly reduced within a period of two to three weeks.

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**Melasmas or hyperpigmentations form in a variety of ways.**

They are triggered by miscellaneous endogenic and exogenous influences such as:

1. UV radiation of the sunlight

2. photosensitization, or in other words, the reduced sensitivity threshold of the skin to light caused by essential oils for instance.

3. hormonal influences, as for example during pregnancy.

4. inflammation mediators such as prostaglandins and cytokines (post- inflammatory hyperpigmentation).

5. AGE (Advanced Glycation Endproducts), or in other words, products that form in the body due to the reaction of proteins or lipids with carbohydrates; they are held responsible for a variety of health implications.

6. other deposits of endogenous metabolic products

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**Mechanism of action of tranexamic acid (TXA) in Melasma**

- Tranexamic Acid prevents UV-induced pigmentation by interfering with the structure of plasminogen and preventing the binding of plasminogen to the lysine-binding sites of keratinocytes.
- The consequences of such event are less free arachidonic acid leading to a reduced ability to produce prostaglandins and thus decreased melanocyte tyrosinase activity and melanogenesis.
- Also, action of Tranexamic Acid on angiogenesis via plasmin could also play a contributory role in its action on melasma.
- Blocking of the Sc-uPA pathway may be another mechanism through which Tranexamic Acid reduces hyperpigmentation.
- Tranexamic Acid is found to be similar to tyrosine in the part of its structure, which can competitively inhibit the activity of tyrosinase.

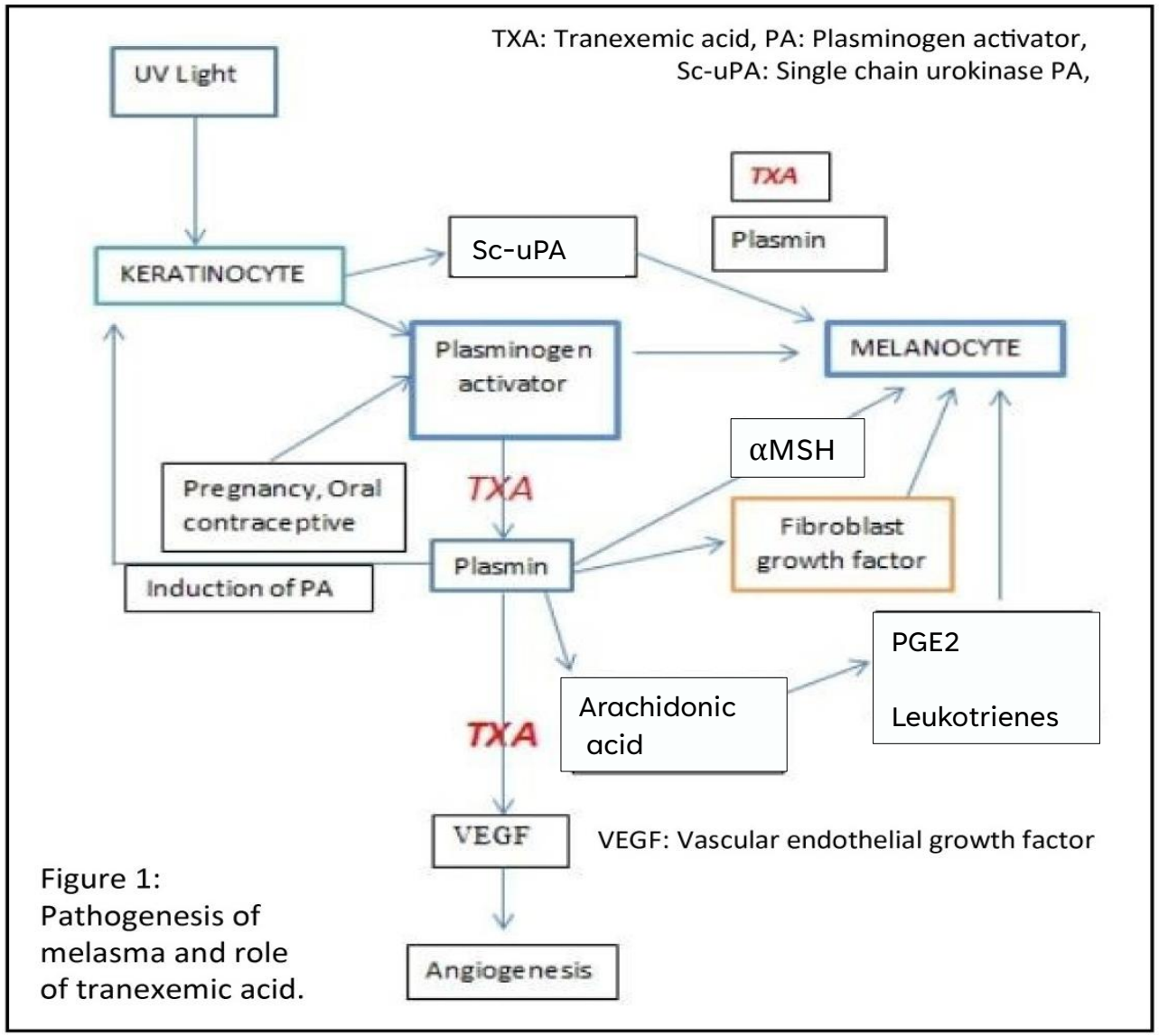


Figure 1: Pathogenesis of melasma and role of tranexemic acid.

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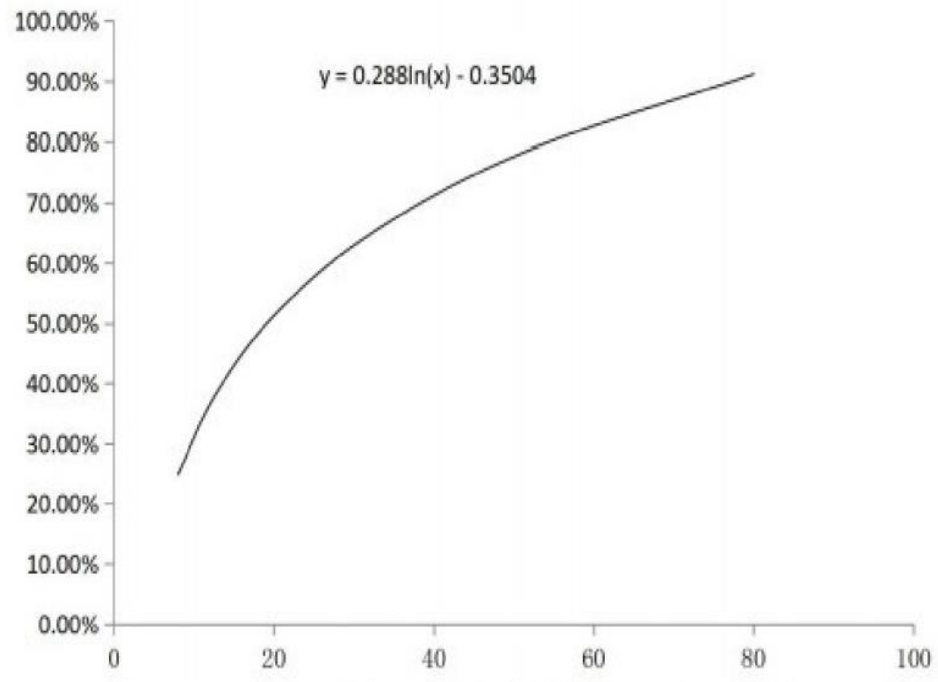
**In-Vitro test-Inhibiting Effect of Tranexamic Acid on Tyrosinase Activity**

| SAMPLE | EC50 ( mg/ml) |
|---|---|
| Tranexamic Acid | 3,832 |




The concentration of Tranexamic acid (mg/mL)

**Conclusion**

Through determination of tyrosinase activity inhibition, the result shows that TA (Tranexamic acid) EC50 value is 3.832mg/ml

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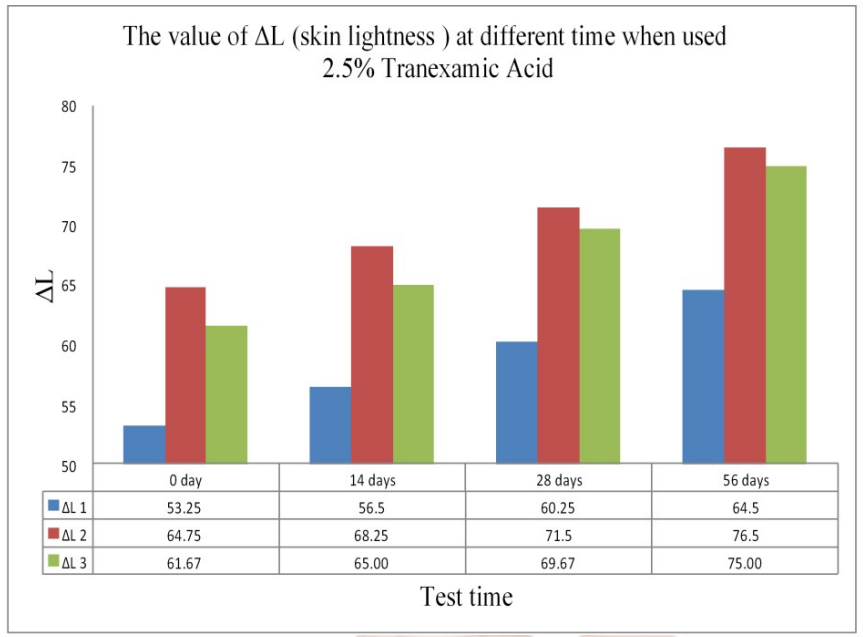
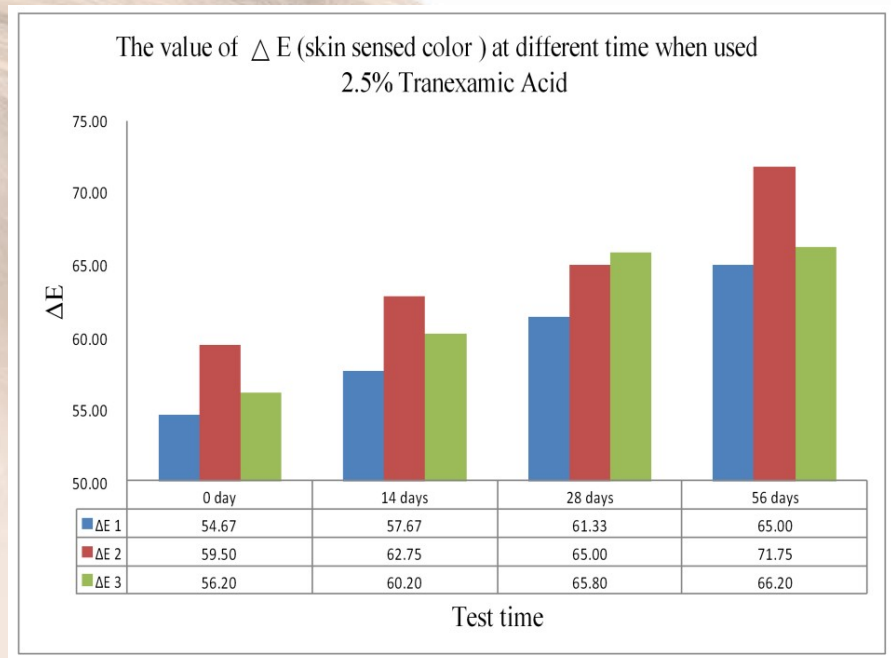
**In-ViVo test-Skin Lightening & Whitening Results**

The ∧L and ∧E  when using 2.5% Tranexamic Acid, comparing with the untreated.




| | 0 day | 14 days | 28 days | 56 days |
|---|---|---|---|---|
| ΔL 1 | 53.25 | 56.5 | 60.25 | 64.5 |
| ΔL 2 | 64.75 | 68.25 | 71.5 | 76.5 |
| ΔL 3 | 61.67 | 65.00 | 69.67 | 75.00 |




| | 0 day | 14 days | 28 days | 56 days |
|---|---|---|---|---|
| ΔE 1 | 54.67 | 57.67 | 61.33 | 65.00 |
| ΔE 2 | 59.50 | 62.75 | 65.00 | 71.75 |
| ΔE 3 | 56.20 | 60.20 | 65.80 | 66.20 |

Comparing with the untreated, skin lightness improved significantly. Skin lightness improved by 7.83% after14 days, 12.11% after 28 days, 20.22% after 56 days by treating with 2.5% Tranexamic Acid.

Comparing with the untreated, skin sensed color improved significantly, skin whiteness improve 6.02% after 14days, 12.77% after 28days, 19.12 % after 56 days by treating with 2.5% Tranexamic Acid.

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**Gluconolactone** also known as Glucono-delta-lactone (GDL), is a lactone of D-gluconic acid. It can be used as a sequestrant, an acidifier, or a curing, pickling, or leavening agent.
GDL is a food additive with the E-number (E575) and is pH-neutral, but hydrolyses in water to gluconic acid which is acidic, adding a tangy taste to foods, though it has roughly a third of the sourness of citric acid.
The yeast Saccharomyces bulderi can be used to ferment gluconolactone to ethanol and carbon dioxide. Thus gluconolactone is biodegradable.

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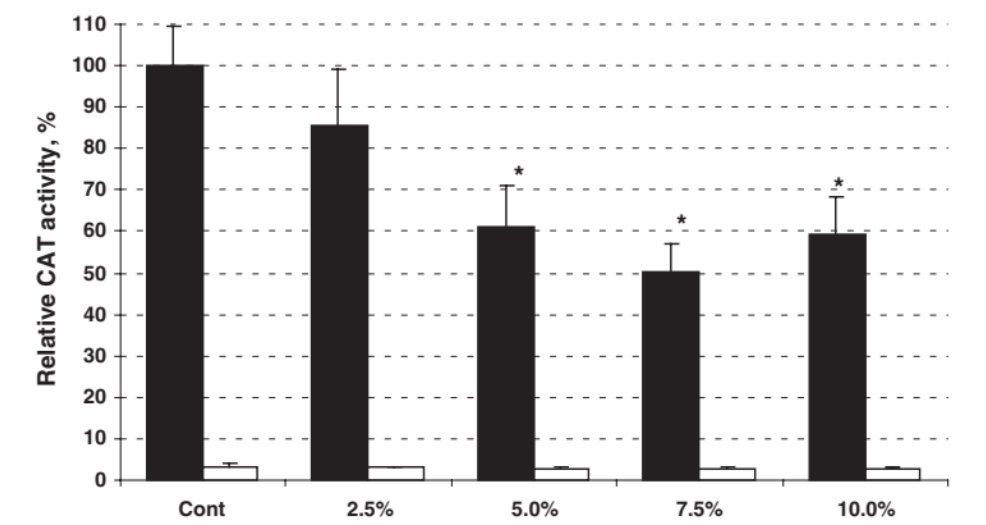
## Protection of Gluconolactone Against Ultraviolet Radiation (in vitro)-Results

Up to one third of the UV may be screened by gluconolactone; however, gluconolactone provides far greater protection when in contact with the cells, delivering most of its protection through other means, possibly by its ability to function as a free radical scavenger.




Gluconolactone alone did not alter CAT activity to a significant degree, resulting in CAT activities of 1.0±0.3-, 1.1±0.1-, 1.0 ±0.1-, and 1.0±0.1-fold (mean±SD) that of untreated cells for gluconolactone concentrations of 2.5%, 5.0%, 7.5%, and 10.0%, respectively. UVB alone increased CAT activity 38.5 ±6.5-fold over unirradiated cells for a UVB dose of 5 mJ/cm2.

*Figure 8. Gluconolactone protects against the UV-induced increase in elastin promoter activity. Fibroblasts, derived from skin containing the human elastin promoter/CAT construct, were incubated with shown concentrations of gluconolactone and then exposed to 5 mJ/cm2 of UVB. Untreated control cells received no gluconolactone. Open rectangles are untreated fibroblasts (Cont) and fibroblasts treated with 2.5%, 5.0%, 7.5%, and 10.0% of gluconolactone and receiving no UVB. Overall, gluconolactone administered 15 minutes before fibroblast irradiation afforded up to 50% protection against UVB. Error bars indicate mean +/- SD. These results are statistically significant at the p<0.001 where indicated with asterisks.*

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## Protection of Gluconolactone Against Ultraviolet Radiation (in vitro)-Results

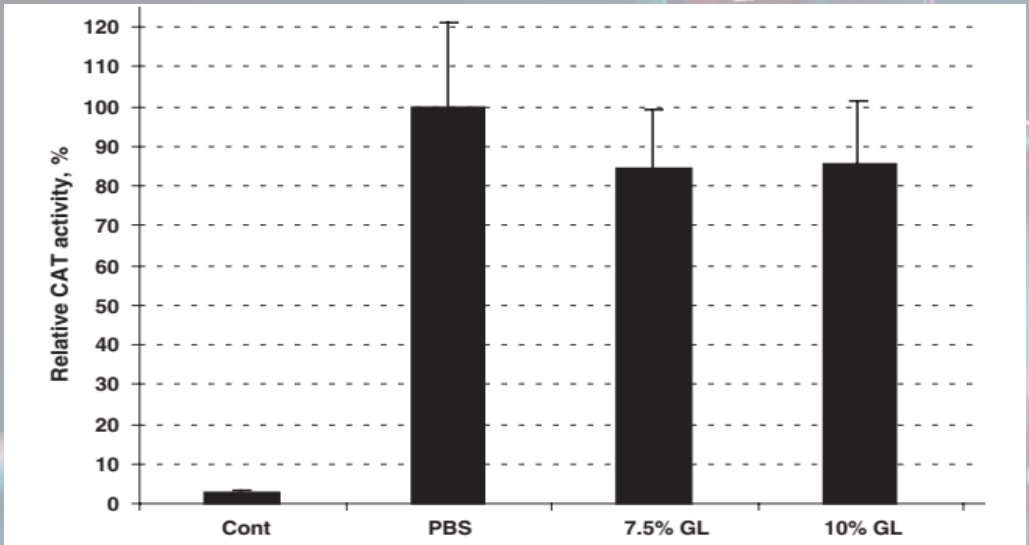


Figure 9. Gluconolactone screened some UVB and reduced CAT activity when compared with PBS alone. To assess the screening ability of gluconolactone, 5 mJ/cm2 of UVB was delivered to the fibroblasts through quartz dishes containing solutions of both 7.5% and 10.0% gluconolactone (GL) in PBS and PBS alone. Relative CAT activity was reduced to 84.5 +/- 14.9% and 85.8 +/- 15.9% by gluconolactone concentrations of 7.5% and 10.0%, respectively. Error bars indicate mean +/- SD.

The lower Relative CAT activity is, the better protection of GDL provided.

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## Protection of Gluconolactone Against Ultraviolet Radiation (in vitro)-Results

- Gluconolactone absorbs only slightly between 250 and 430 nm. Absorption decreases significantly above 350 nm.
- Thus GDL can be incorporate into UV protective and sunscreen products. And this UV-protective effect has concentration-dependent relationship, i.e. the higher concentration of GDL is, the better UV-protective efficacy is.
- GDL thus can be used in photo-sensitive and photo-aging formulations.

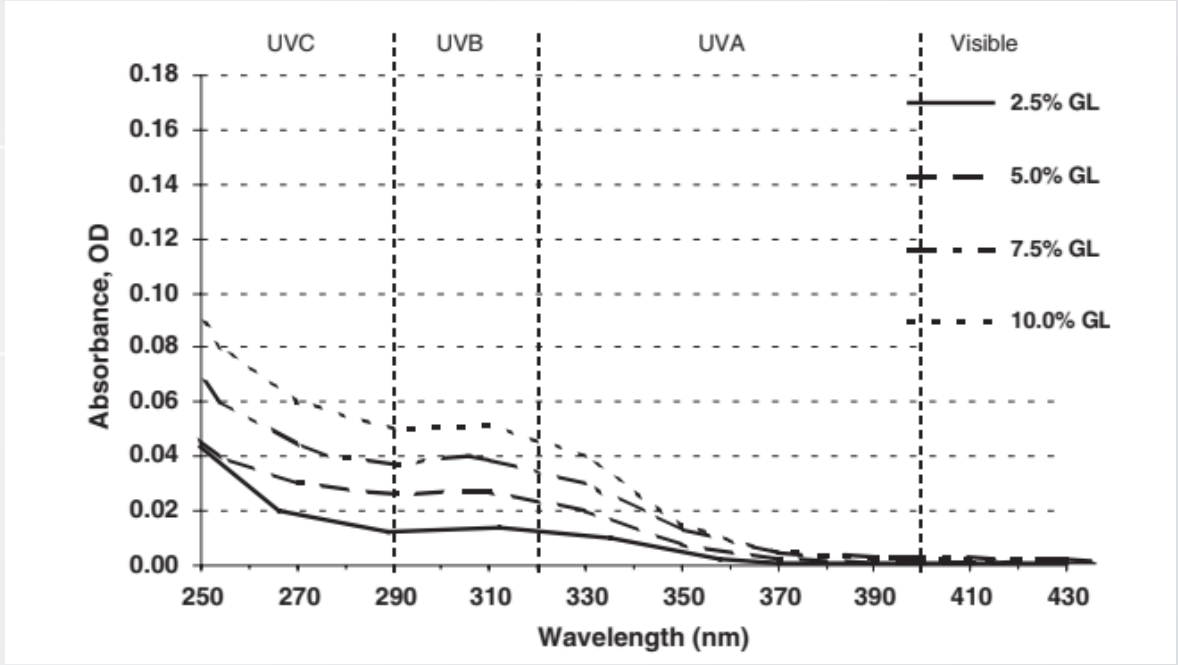


*Figure 10. Gluconolactone absorbs slightly (optical density [OD] less that 0.1) in the UVC and UVB region (250 to 320 nm), and this absorption drops down to approximately baseline in the UVA (320 to 400 nm) and visible (more than 400 nm) range.*

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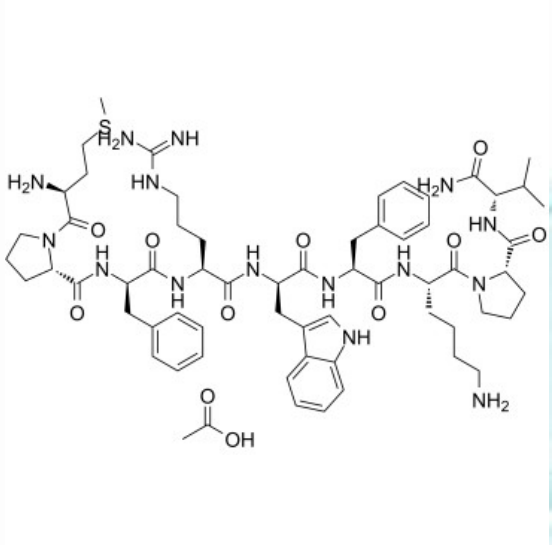

*Fig.1 Structure diagram of Nonapeptide-1*

**Nonapeptide-1** is a bionic peptide that has a good match with the melanocortin 1 receptor (MC1R) on melanocytes, so it can act as a antagonist of melanocyte-stimulating hormones (MSH) and competitively bind to the MC1R, preventing tyrosinase from being further activated to produce melanin.

- Competitively block the receptors and entries of various signal factors on melanocytes.
- Weakened the activity of melanocyte, reducing melanin production.
- Effectively inhibit the production of melanin from the source, brightening skin.

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## What is melanocyte-stimulating hormones (MSH) ?

- Melanocytes in skin make and secrete MSH (α-/β-/γ-) in response to ultraviolet light, where it increases synthesis of melanin.
- Acting through melanocortin 1 receptor (MC1R), α-MSH stimulates the production and release of melanin (melanogenesis) by melanocytes in skin and hair.
- Acting in the hypothalamus, α-MSH suppresses appetite. α-MSH secreted in the hypothalamus also contributes to sexual arousal.

**For Animals (In amphibians):**

For some animals, such as the claw-toed frog Xenopus laevis , the rate of MSH synthesis increases in a dark/dim environments. This causes pigment to be dispersed in pigment cells in the toad's skin, making it become darker, and harder for predators to spot. The pigment cells are called melanophores and therefore, in amphibians, the hormone is often called melanophore-stimulating hormone (MSH).

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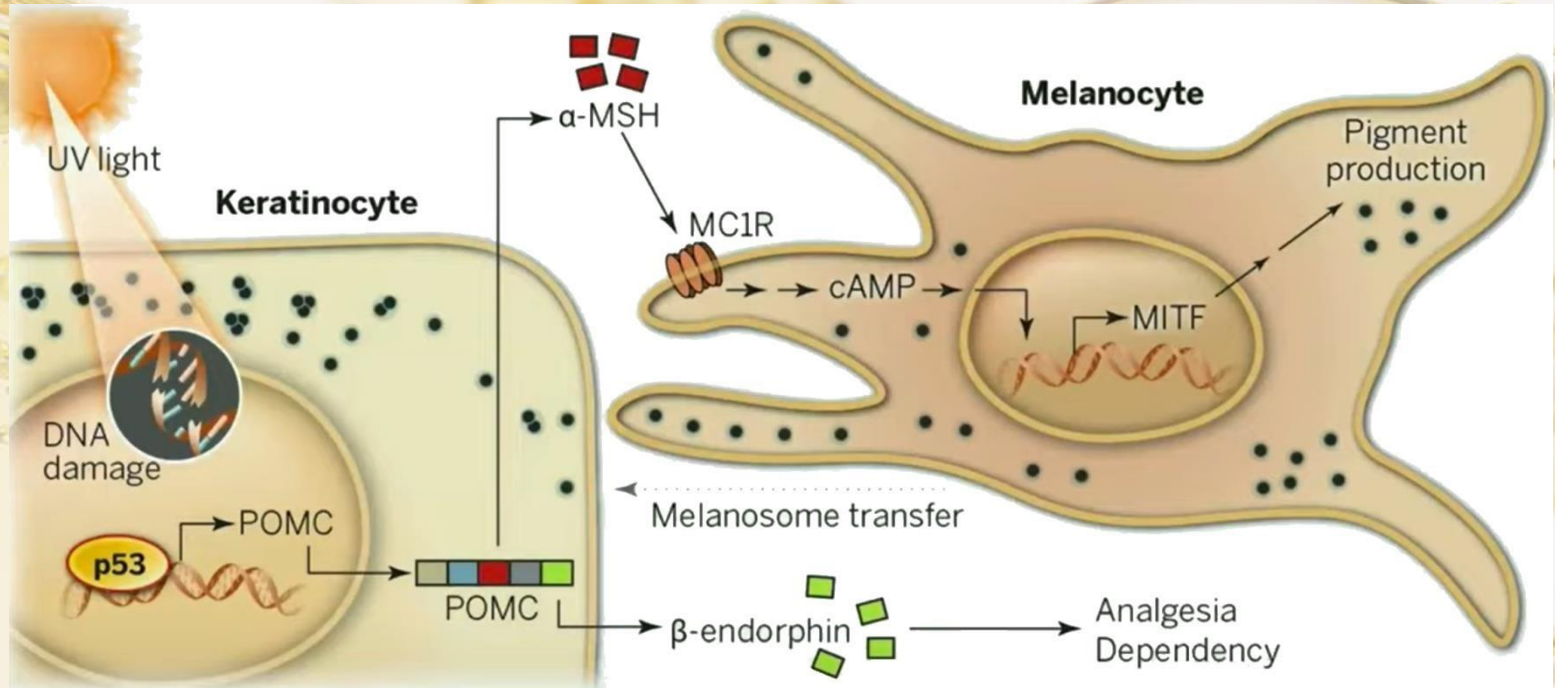
**The Acting Mechanism of Nonapeptide-1:**



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**Features of Nonapeptide-1:**

- Biomimetic and Potent α-MSH antagonists (with an IC50 value of 11 +/- 7 nM.
- Competitively binding MC1R and blocking α-MSH to bind MC1R, reducing the production of melanin.
- Work fast through directly inhibiting melanin-forming pathways in melanocyte, ahead of activation of tyrosinase.
- Not only inhibit overproduction of melanin, but also reduces melanin deposition.
- Tackle the root of lightening problems, brightening skin inside out.
- Help energizing mitochondria and regulates circadian rhythms.
- Can be used day or night for daily skin care.

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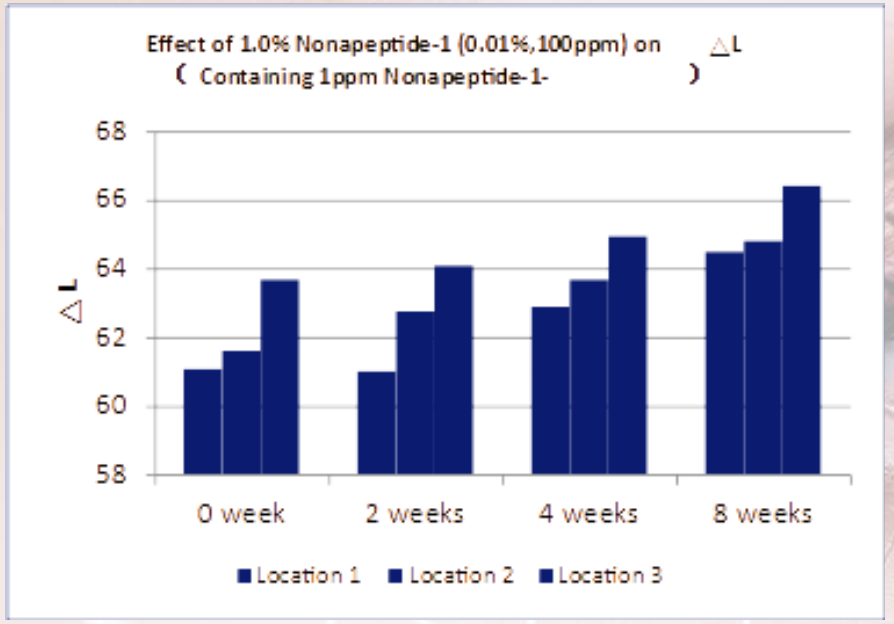
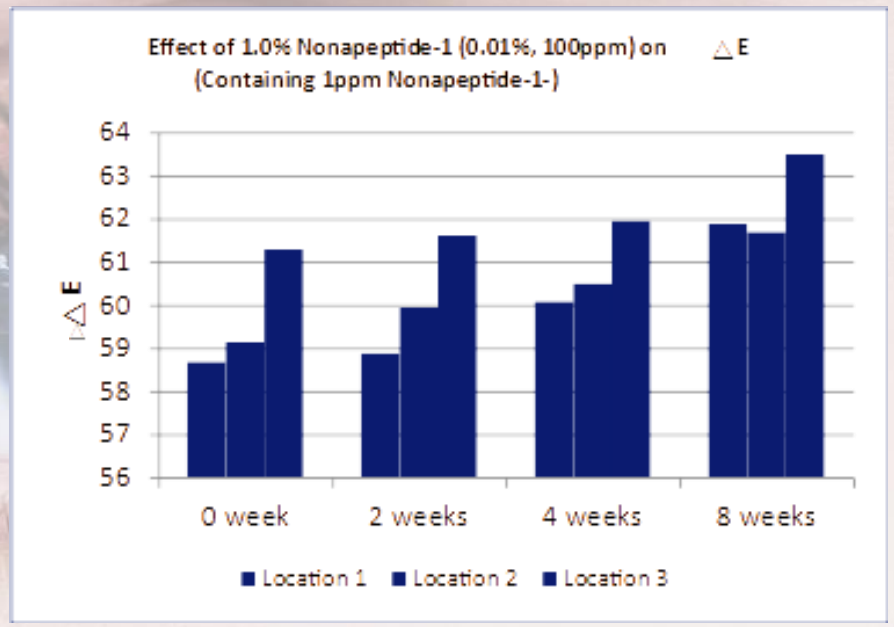
## Clinical Test-Lightening test of 1% Nonapeptide-1 (0.01%)

(active:Nonapeptide-1 (0001%)




*the higher the △ L value indicates the better skin lightening effect, the higher △ E indicates the better comprehensive skin performance.*

**Summary:**

- The average value of △ L was 62.11 before use. After using for 28 days, the △ L increased by 5.01% at the 56th day compared with initial state.
- The average value of △ E was 59.69 before use. After using for 28 days, the △ E increased by 4.43% at the 56th day compared with initial state.

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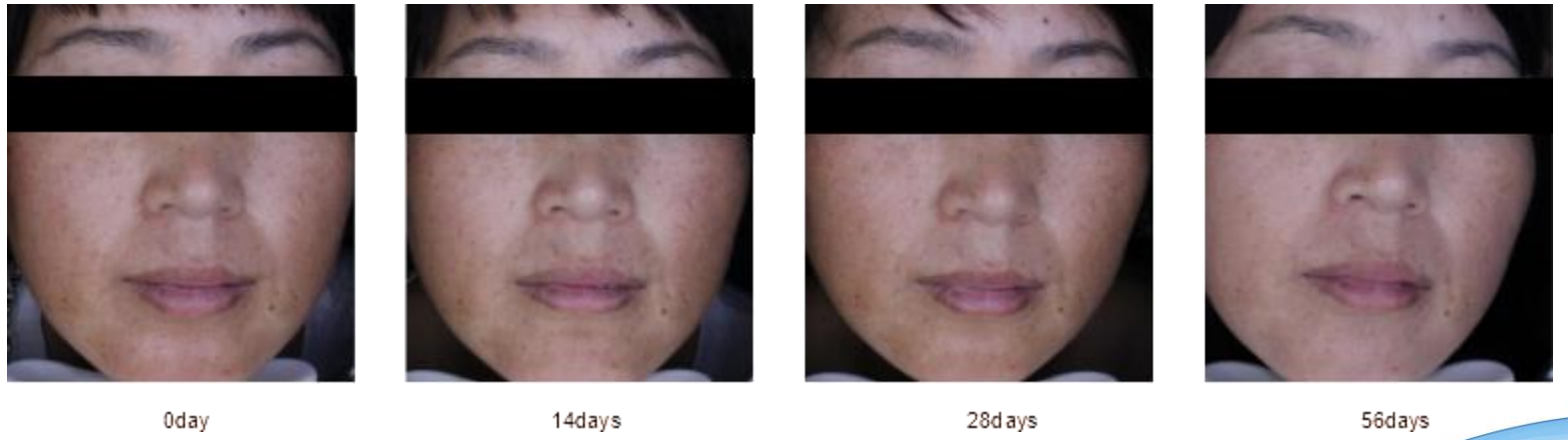
## Clinical Photos-Lightening Test (Typical Subject)

1.0% Nonapeptide-1 (0.01%,100ppm) , Equals to NOnapeptide-1 —at 0.0001%



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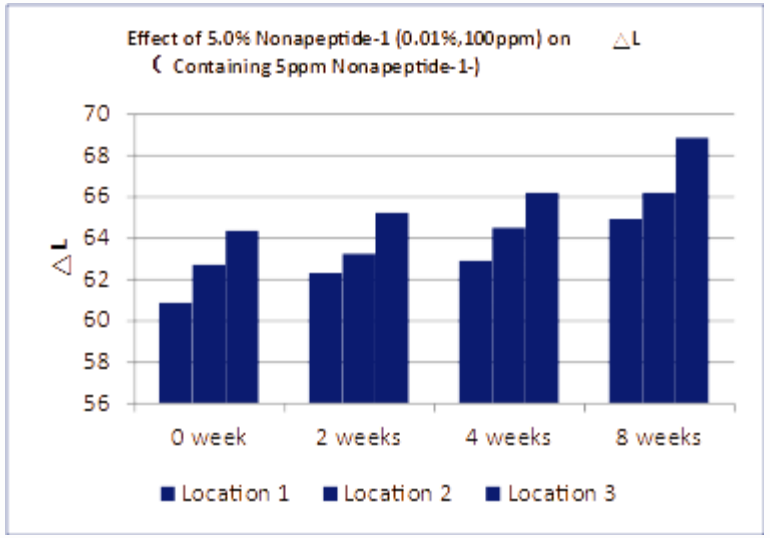
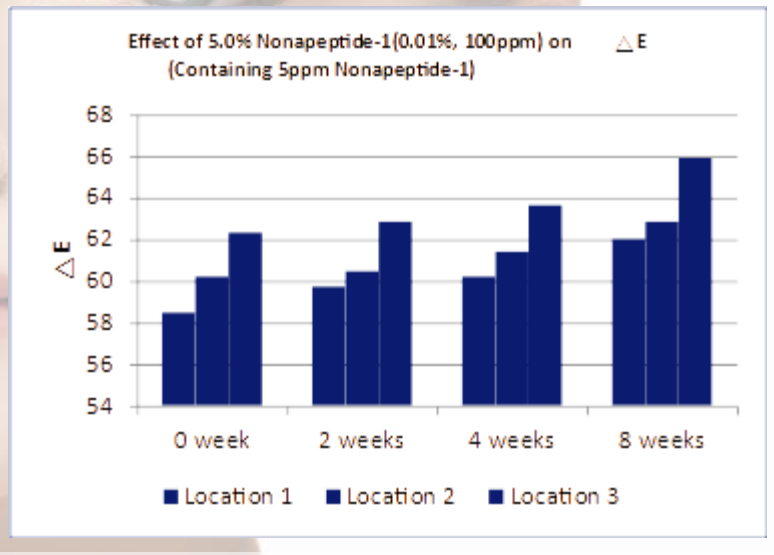
## Clinical Test-Lightening test of 5% Nonapeptide-1 (0.01%)

ACTIVE (N1P-0.0005%)




*the higher the △ L value indicates the better skin lightening effect, the higher △ E indicates the better comprehensive skin performance.*

**Summary:**

- The average value of △ L was 62.61 before use. After using for 28 days, the △ L increased by 6.42% at the 56th day compared with initial state.
- The average value of △ E was 60.33 before use. After using for 28 days, the △ E increased by 5.39% at the 56th day compared with initial state.

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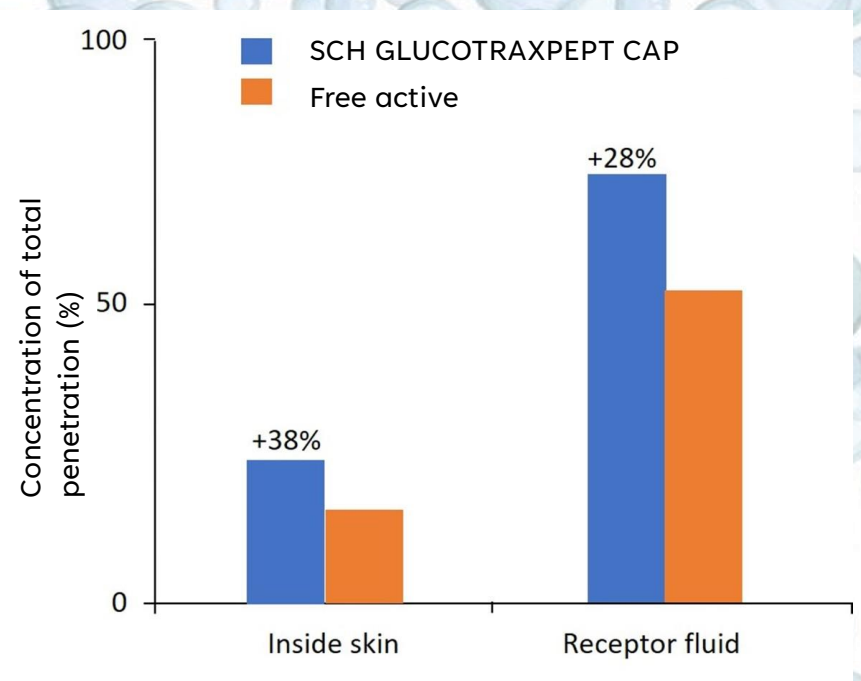
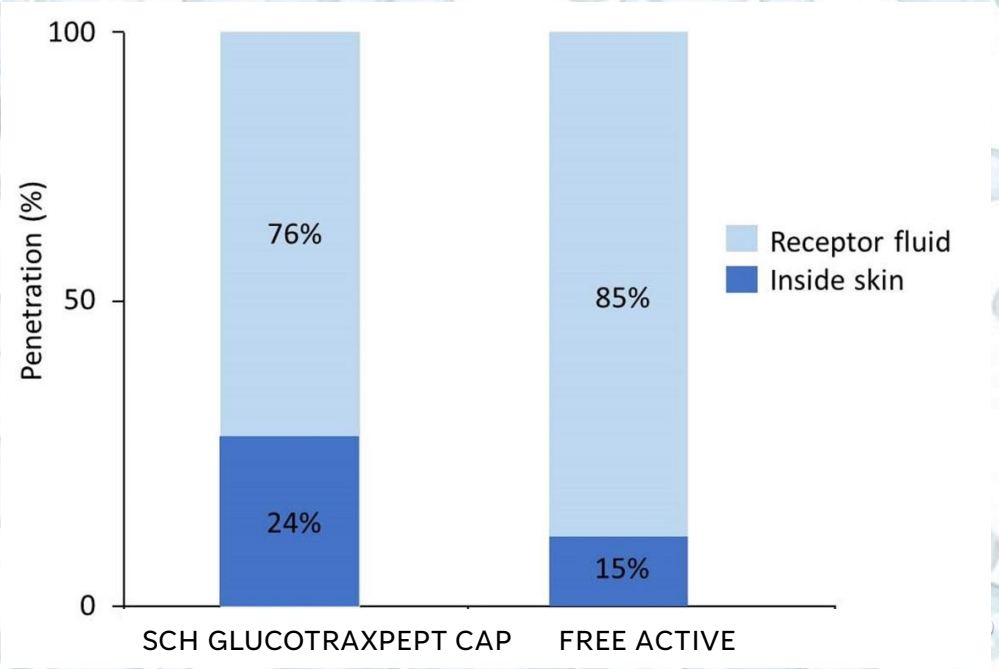
**Qualitative analysis of penetration and skin retention.**

The skin penetration of SCH GLUCOTRAXPEPT CAP capsules have shown the ability to penetrate an average of 30% more than free active administrated alone. Normalizing the total penetrated amounts of all data collected by the quantitative analysis, the relative expression values were 24% and 15% retained inside the skin and 76% and 85% in the receptor fluid.

(Fig 2 and Fig 3).

Fig 2. Penetration at 20 h after application.



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**Speed and depth of penetration into the skin.**

There was found a fast and deep penetration of SCH GLUCOTRAXPEPT CAP within skin at 20h of topical application. At 1h of application, capsules started penetrating skin Dermis zone. At 20h, it was much deeper in the Dermis, while when free active was applied in free form it was seen that they remained on the surface of the skin. (Figure 4).

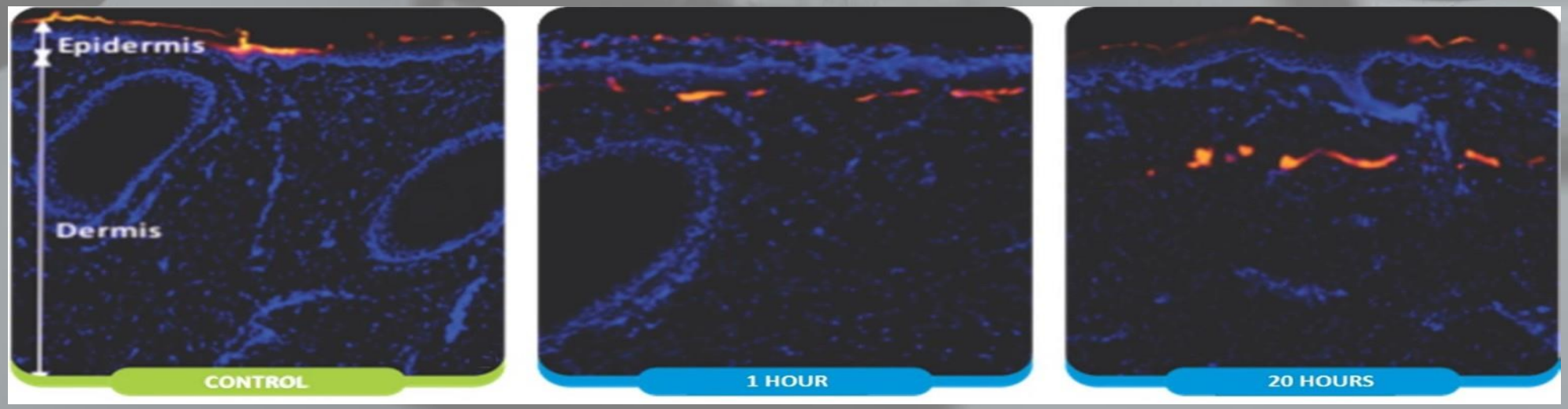


Fig 4. Confocal microscopy images of skin slices at 0, 1 and 20h.

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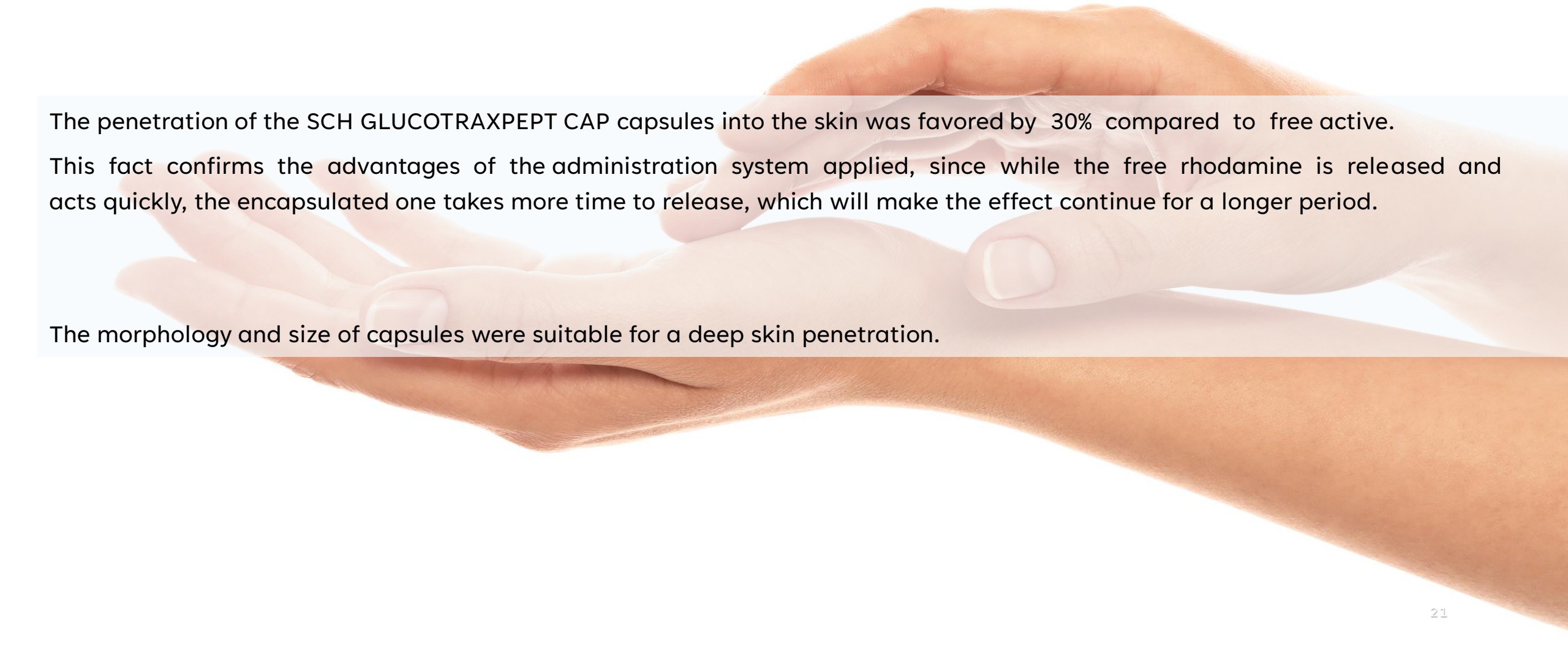
## Conclusions

The penetration of the SCH GLUCOTRAXPEPT CAP capsules into the skin was favored by 30% compared to free active.

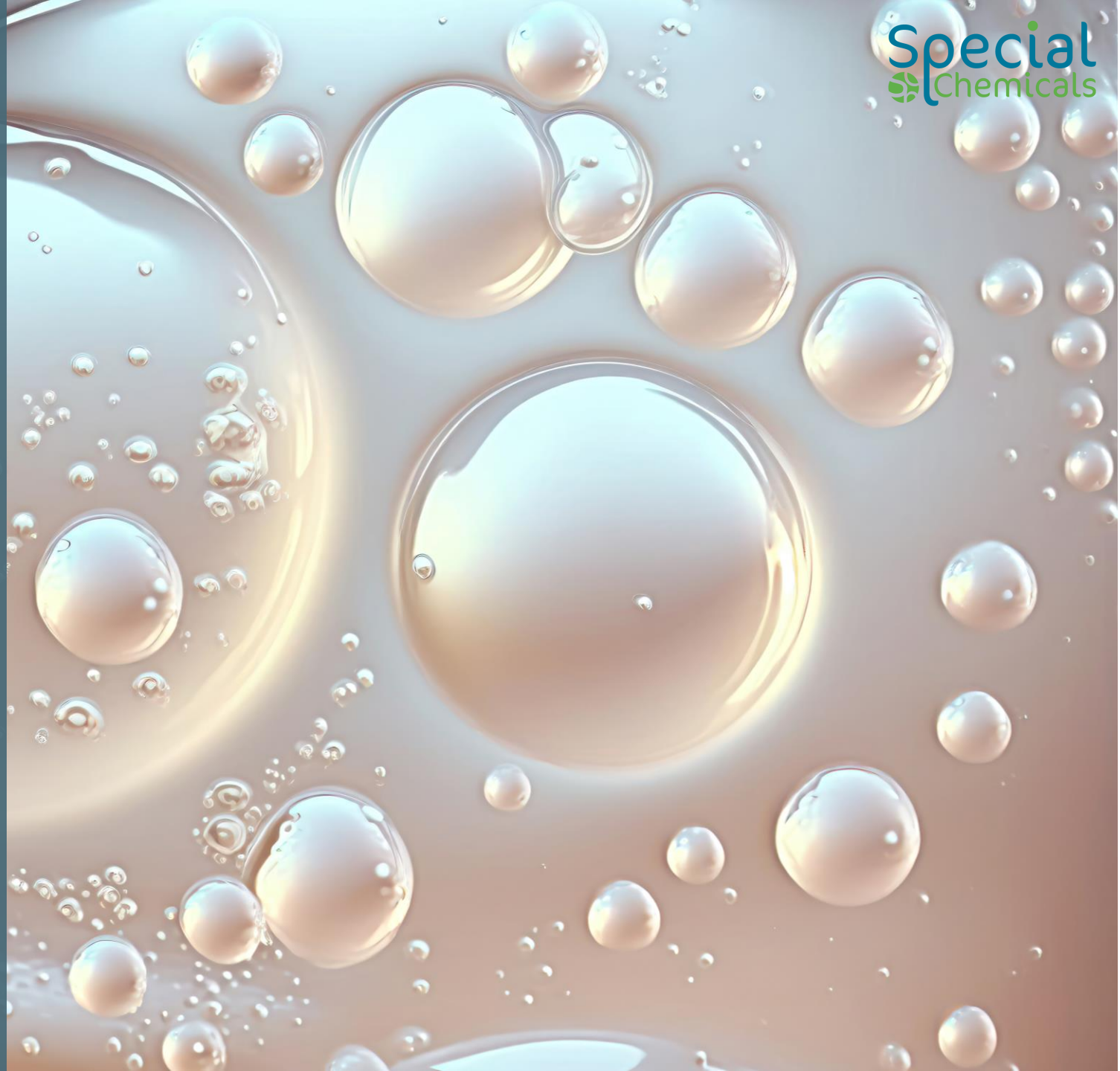
This fact confirms the advantages of the administration system applied, since while the free rhodamine is released and acts quickly, the encapsulated one takes more time to release, which will make the effect continue for a longer period.

The morphology and size of capsules were suitable for a deep skin penetration.



# SPECIFICATIONS

- Apperance: Viscous Solution
- INCl.: Water, tranexamic acid, gluconolactone, nonapeptide-1, xanthan gum, Polycaprolactone, polyvinyl alcohol, sorbitan stearate
- Solubility: Dispersible in water
- Recommended dose: 5%
- Legal status: EUROPE, CHINA, USA



Special Chemicals

# THANK YOU

*Thank you for your interesting and attention!*
*If you need sample and technical data, please contact us without hesitation*

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